

REMARKS

This Amendment is filed in response to the Office Action issued February 10, 2003. A Petition to Extend Time for two (2) months in order to respond to the outstanding Office Action in the above-identified application is attached.

A Supplemental Information Disclosure Statement, Form PTO-1449, and a copy of each cited reference is being submitted along with this Amendment, along with the appropriate fee.

Formal drawings are attached.

Claims 1-27 were pending in this application.

Claims 22, 23 and 27 are canceled, without prejudice. Applicants reserve the right to pursue this and any other subject matter disclosed in this specification in one or more future continuing applications.

Claims 1, 2, 5, 6, 8-10, 13, 14, 18, 19, and 26 are amended to both correct editorial oversights as well as to more particularly point out and distinctly claim this portion of Applicant's invention.

Claim 1 was amended to correct several editorial oversights as well as to recite better antecedent basis for the term --helper dependent adenoviral vector--.

Claims 2, 13, 14, and 26 are amended to correct editorial and/or spelling oversights.

Claim 10 is amended to enter a complete Markush grouping as well as to provide the appropriate antecedent basis for dependent claims 13 and 14.

Claims 5 and 6 are amended to provide proper antecedent basis.

Claims 8, 9, 18, 19 are amended, and claim 10 is further amended, to recite--first genic unit-- as opposed to "first unit."

No new matter is added by amendment to claims 1, 2, 5, 6, 8, 9, 10, 13, 14, 18, 19, and 26.

Objection to Claims 22 and 23 Under 37 C.F.R. 1.75 (c)

Claims 22 and 23 are objected to under 37 C.F.R. 1.75 (c) allegedly "as being of improper dependent form for failing to further limit the subject matter of a previous claim." Applicants respectfully traverse, rendering this objection moot, by canceling claims 22 and 23, without prejudice. Applicants respectfully reserve the right to pursue canceled subject matter in a future continuing application. Accordingly, Applicants respectfully request reconsideration of this objection.

Rejection of Claims 1-27 Under 35 U.S.C. §112, Second Paragraph and §101

Claims 1-27 stand rejected under 35 U.S.C. 112, second paragraph. The Examiner takes the position that the term "genetic" as used throughout the pending claims gives "a meaning repugnant to the usual meaning of that term." More specifically, the Examiner takes the position that use of the term "genetic" is inappropriate and instead should be "polynucleotide sequences", presumably because "the polynucleotide sequences of interest in the invention is drawn to adenovirus which do not contain chromosomes...". Applicant respectfully disagree with this reasoning. First, the instant claims are not drawn to adenovirus or adenovirus vectors, but instead to the cells which contains these introduced "genetic units." Second, Applicants respectfully take the position that the term "genetic" as it applies to adenoviral-based sequences is, as opposed to the Examiner's position, wholly appropriate. More specifically, Applicant asserts that virus (including adenovirus) are recognized in the art as having genetic material, or "chromosomes." Please find select pages (including the title, and chapter page) from two noted texts in the field (Molecular Biology of the Cell, *Id.*, and *Fundamental Virology*, Third Edition, Bernard N. Fields *et al.*, *Eds.*) [attached as pages 1-11 of Exhibit A]. The language contained therein specifically speaks to the subject of viral genetic material and the concept of "viral chromosomes" (*see*, particularly pages 274 (6th and final full paragraph)-277 of the former; and pages 983-985 of the latter. This can be gleaned from the following excerpt:

The genetic information of a virus can [] be carried in a variety of unusual forms, including RNA instead of DNA. A viral chromosome may be a single-stranded RNA chain, a double-stranded RNA helix, a circular single-stranded DNA chain, or a linear single-stranded DNA chain.

Pages 276-277, *Molecular Biology of the Cell*, *Id.*

It is also appreciated that such viral chromosomes are composed of specific genetic (or genetic) units.

All adenovirus genomes that have been examined to date have the same general organization, i.e., the genes encoding specific functions are located at the same position on the viral chromosome, ...

Page 983, *Fundamental Virology*, Id.

With this basis in the art for the concept of the viral chromosome and its constituent nucleic acid, Applicants submit that the term “genic” or “genetic” in reference to the nucleic acid sequence of the claims is wholly appropriate in the context in which it is used. The claims, therefore, meet the standard set out in 35 U.S.C. §112, second paragraph, by particularly pointing out and distinctly claiming the subject matter which Applicants regard as the invention, particularly to one of skill in the pertinent art. Accordingly, Applicants respectfully request reconsideration and withdrawal of the instant rejection.

Claim 27 is further rejected under §§ 112, second paragraph and 101 for various reasons detailed in Paper No. 15. Applicants respectfully traverse this rejection by cancellation of claim 27. Applicants respectfully reserve the right to pursue canceled subject matter in a future continuing application. Accordingly, Applicants respectfully request reconsideration of these objections and §§112, second paragraph and 101 rejections of claims 1-27.

Rejection of Claims 22 and 23 Under 35 U.S.C. §102(b)

Claim 22 stands rejected under 35 U.S.C. §102 (b) allegedly as “being anticipated by Alemany et al. (Journal of Virological Methods, 1997).” Claim 23 stands rejected under 35 U.S.C. §102 (b) allegedly as “being anticipated by Yeh et al. (Journal of Virology, 1996).” Applicants respectfully traverse, rendering this objection moot, by canceling claims 22 and 23, without prejudice. Applicants respectfully reserve the right to pursue canceled subject matter in a future continuing application. Accordingly, Applicants respectfully request reconsideration of this objection.

Now pending claims 1-21 and 24-26 are in proper form for allowance. Early action to that end is earnestly solicited. The Examiner is invited to contact the undersigned attorney if clarification is required on any aspect of this response, or if any of the claims are considered to require further amendment to be placed in condition for allowance after entry of this Amendment.

Respectfully submitted,



Anna L. Cocuzzo
Reg. No. 42,452
Attorney for Applicants
Merck & Co., Inc.
P.O. Box 2000
Rahway, NJ 07065-0907
(732) 594-1273

Date: July 10, 2003

CURRENT STATUS OF CLAIMS

1(amended). Cells for the production of helper dependent adenoviral vectors, including at least the following genic units:

- a first genic unit comprising an adenovirus defective genome having the inverted terminal repeats in head-to-tail configuration, the encapsidation signal inactivated, and at least one of the non-structural regions inactivated;

- a second genic unit ~~units~~ comprising at least one inducible promoter and at least one of the regions inactivated in the first genic unit, said regions being under the control of said inducible promoter;

whereby following the activation of the inducible promoter of the second genic unit and the infection of the cells with said helper dependent adenoviral vectors, the first genic unit and the second genic unit enable the production of said helper dependent ~~defective~~ adenoviral vectors in said cells in absence of helper vector.

2(amended). Cells according to claim 1, wherein the first genic unit is integrated in the genome of the cells and has at both the extremities inverted ~~Inverted~~ terminal repeats ~~Repeats~~ in head-to-tail configuration.

3(original). Cells according to claim 1, wherein the first genic unit is included in an episomal unit including an element enabling the replication of said episomal unit in a low number of copies.

4(original). Cells according to claim 3, wherein said element enabling the replication of said episomal unit is the origin of replication of a virus.

5(amended). Cells according to claim 4, wherein the gene coding for an the activating factor of said origin of replication is further included in the episomal unit.

6(amended). Cells according to claim 4, wherein the gene coding for an the activating factor of said origin of replication is integrated in the genome.

7(previously amended). Cells according to claim 4, wherein said virus is Epstein-Barr virus, the origin of replication is OriP and the activating factor is EBNA-1.

8(amended). Cells according to claim 1, wherein the encapsidation signal of the adenovirus defective genome of the first genic unit is inactivated by total or partial deletion.

9(amended). Cells according to claim 1, wherein the non-structural regions of the adenovirus defective genome of the first genic unit is inactivated by total or partial deletion.

10(amended). Cells according to claim 1, wherein the inactivated regions of the first genic unit are selected from the group consisting of E1, ~~E2~~ E2A, E2B, and E4.

11(original). Cells according to claim 10, wherein said regions are E1 and E4.

12(original). Cells according to claim 10, wherein said regions are E1, E4 and E2A.

13(amended). Cells according to claim 10, wherein said regions are E1, E4 and E2B ~~E2b~~ polymerase.

14(amended). Cells according to claim 10, wherein said regions are E1, E4 and E2B ~~E2b~~ preterminal protein (PTP).

15(previously amended). Cells according to claim 1 wherein the viral regions of the first genic unit is operatively linked to at least one regulatory element enabling the tight control of the expression of said regions.

16(previously amended). Cells according to claim 1 wherein the promoter on the second genic unit is the tetracycline operator.

17(previously amended). Cells according to claim 1 wherein the viral regions in the second genic unit are operatively linked to elements regulating the expression of said regions.

18(amended). Cells according to claim 1 wherein the adenovirus defective genome of the first genic unit is totally or partially constituted by the genome of a human adenovirus.

19(amended). Cells according to claim 18, wherein said adenovirus defective genome of the first genic unit is totally ~~o~~ or partially constituted by the genome of at least one of the human adenoviruses Ad2 and Ad5.

20(previously amended). Cells according to claim 1, wherein the viral regions of the second genic unit, are totally or partially constituted by the viral regions of a human adenovirus.

21(original). Cells according to claim 20, wherein said viral regions of the second genic unit, are totally or partially constituted by the viral regions of at least one of the human adenoviruses Ad2 and Ad5.

22-23(canceled).

24(previously amended). The cells according to claim 1, wherein said cells are mammalian cells.

25(original). The cells according to claim 24, wherein said mammalian cells are human cells.

26(amended). Compositions comprising the cell of claim 1, a vehicle or a carrier, ~~characterised~~ characterized in that said composition is free of contaminating helper viruses.

27(canceled).